Toward Cholera Elimination, Haiti

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This study describes the apparent discontinuation of cholera transmission in Haiti since February 2019. Because vulnerabilities persist and vaccination remains limited, our findings suggest that case-area targeted interventions conducted by rapid response teams played a key role. We question the presence of environmental reservoirs in Haiti and discuss progress toward elimination.

fter cholera was reintroduced into Haiti in 2010 (1), the country experienced an epidemic of unparalleled magnitude: the 9,789 recorded casualties represent the largest number for a single epidemic in the past 20 years (http://apps.who.int/gho/data/ node.main.174). Unfortunately, vulnerabilities of people in Haiti to fecal-oral diseases such as cholera have barely been reduced over the past decade. The National Plan for the Elimination of Cholera 2013-2022 aimed to improve access to drinking water to >85% of the population, access to sanitation to >90% of the population, and access to healthcare to >80% of the population (2). However, these indicators improved very slowly or even deteriorated during 2012-2017 (3). The country still faces a deep economic and social crisis and has also endured several natural disasters. such as Hurricane Matthew in October 2016. In addition, the Multi-Partner Trust Fund set in December 2016 by the United Nations to support the response

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to cholera in Haiti gathered only US \$20.8 million during 2016–2020 (http://mptf.undp.org/factsheet/fund/CLH00).

To alleviate these persisting vulnerabilities and eliminate cholera transmission, experts and public health institutions have appealed to expand mass use of oral cholera vaccines (OCV) (4,5). Meanwhile, a nationwide coordinated rapid response strategy structured around case-area targeted interventions was gradually implemented beginning in July 2013 by the Ministry of Public Health and Population of Haiti (MOH), UNICEF, and other partners (6). Analogous to forest fire management, the strategy aimed to rapidly detect local outbreaks and send rapid response teams, mostly composed of nongovernmental organization and MOH staff, to the households and neighbors of infected persons (Appendix, https://wwwnc.cdc.gov/EID/ article/27/11/20-3372-App1.pdf). This study aims to describe and decipher the progress of cholera control in Haiti.

The Study

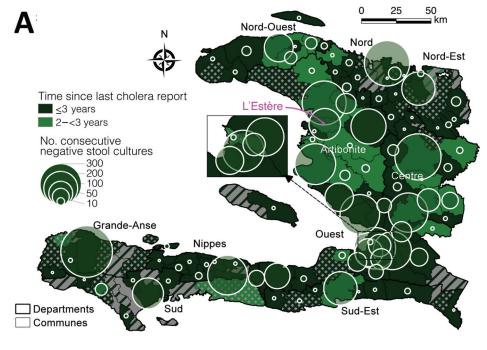
We analyzed cholera surveillance data routinely collected since 2010 by the MOH with support of the Pan American Health Organization and the Centers for Disease Control and Prevention, including results of stool cultures searching for Vibrio cholerae O1 (Appendix). The study was approved by the Bioethics National Committee of the MOH (authorization no. 1819-41). Suspected cholera cases stagnated during 2013-2016; the median was 38,733 annual cases (incidence rate 6.9/100,000 person-weeks). Incidence then dramatically decreased to 13,681 cases (incidence rate 2.2/100,000 person-weeks) in 2017, to 3,777 cases (incidence rate 0.6/100,000 person-weeks) in 2018, and to 720 cases in 2019 (incidence rate 0.1/100,000 person-weeks). The last cluster of suspected cholera cases and the last cholera-associated death were observed in the commune of L'Estère, Artibonite department, in February 2019. As of July 1, 2021, a total of 92 (67%) of the 140 communes have not notified a case for ≥ 3 years (Figure 1, panel A). Of note, the last stool culture positive for *V. cholerae* O1 was also sampled in L'Estère on February 4, 2019; none of the 5,223 consecutive stool specimens sampled from diarrheic patients across the country, including 2,255 specimens sampled in 2021, have tested positive since 2019 (Figure 1, panel B). Reports of cholera have thus halted for \geq 3 years in 112 (80%) of communes in Haiti (Figure 1, panel A).

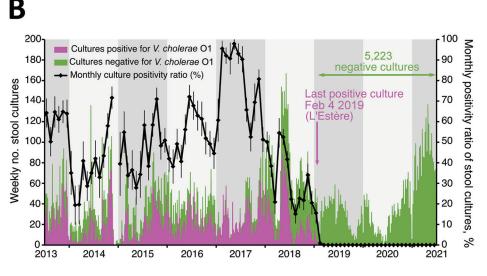
To analyze factors associated with this apparent discontinuation of cholera transmission in February 2019, we compiled data from mass OCV campaigns implemented across Haiti (Appendix). During 2012–

2018, the MOH recorded 33 campaigns targeting 31 communes and 16 prisons (Table 1; Figure 2, panel A). A total of 1,576,209 persons received ≥1 dose. The 2-dose regimen was completed for 74% of these persons, with marked heterogeneity (Figure 2, panel A). Overall, <10% of the population in Haiti has been fully vaccinated (Table 1). Considering the duration of protection of 1-dose and 2-dose regimens of OCVs (7), only 2.4% of persons in Haiti were likely still protected in 2019 (Table 1).

Figure 1. Cholera elimination progress and surveillance effort in Haiti as of July 1, 2021. A) Time elapsed since the last cholera report (i.e., number of years since the last positive culture or last reported suspected cholera case [choropleth colors and patterns]) and of the number of consecutive negative cultures (proportional circles), by commune. Communes with >1 negative culture since the last positive culture or the last reported death are colored with solid green, with elimination time calculated since the last positive culture or suspected cholera death; communes with no stool sampled for culture since the last positive culture or the last reported death are colored with green crosshatching, with elimination time calculated since the last reported suspected cholera case or death: communes with no history of stool sampling for cholera culture but with reported cases are colored with green diagonal hatching, with elimination time calculated since the last reported suspected cholera case or death; and communes with no history of stool sampling and no reported cases are colored in solid gray. Communes are colored according to the time elapsed since possible elimination (i.e., number of years since the last positive culture or the last reported suspected cholera case). The magenta arrow localizes the commune of the last positive stool sample in Haiti. B) Plot of the weekly

number of positive (magenta)





and negative (green) stool cultures for *Vibrio cholerae* O1 and monthly culture-positivity ratio. Data source: Ministry of Public Health and Population of Haiti (pers. comm., 2021 Jul 20; see also Appendix, https://wwwnc.cdc.gov/EID/article/27/11/20-3372-App1.pdf). *V. cholerae* O1, *Vibrio cholerae* O1.

Table 1. Summary of killed whole-cell oral cholera vaccine campaigns, Haiti, 2012–2019*

		No. (%)	No. persons who	No. persons who	Percentage of	Percentage of
	Population in	targeted	received ≥1 OCV	received 2nd OCV	fully vaccinated	population with residual
Year	Haiti	communes	dose	dose (%)	population†	vaccine immunity‡
2012	10,644,927	3	97,774	88,762	0.8%	0.5%
2013	10,937,675	2	113,045	102,250	0.9%	1.0%
2014	11,239,398	8	197,147	188,909	1.7%	1.8%
2015	11,550,392	0	0	0	0.0%	1.5%
2016	11,870,966	18	885,210	106,054	0.9%	1.5%
2017	12,201,437	3	215,358	628,049	5.1%	5.1%
2018	12,542,135	1	67,675	59,537	0.5%	3.9%
2019	12,893,402	0	0	0	0.0%	2.4%
Total	NA	31 (22)	1,576,209	1,173,561 (74)	9.1%	NA

^{*}Data source: Ministry of Public Health and Population of Haiti (pers. comm., 2021 Jul 20; see also Appendix, https://wwwnc.cdc.gov/EID/article/27/11/20-

fully vaccinated persons, and the published protection duration after a 1-dose and 2-dose regimen (Appendix).

We compiled a total of 48,710 case-area targeted interventions recorded by UNICEF during July 2013–December 2019 that were implemented across 139 administrative communes (Table 2; Figure 2, panel B). Of those interventions, ≈71% involved a complete package: house decontamination by chlorine spraying, health education about cholera, distribution of soap and chlorine tablets for household water treatment, and distribution of antibiotic prophylaxis to close contacts of cholera cases. Progress from 2013 to 2019 was strong (Table 2), and spatial heterogeneity was marked (Figure 2, panel B). The overall number of case-area targeted interventions per suspected cholera case was 0.3; this ratio improved markedly during 2013–2019 (Table 2).

Conclusions

As confirmed by an extensive laboratory-based surveillance effort, despite sociopolitical turmoil, the cholera epidemic in Haiti seems to be ending. However, a high-coverage national 2-dose cholera vaccination campaign could not be implemented, because neither the required stockpile nor the funds, estimated at US \$66 million (5), have been available. Although OCV campaigns proved effective in some targeted areas (8), these limited and incomplete campaigns were insufficient to compensate for the global waning of the herd immunity built up during the initial incidence peaks of 2010–2012. In the absence of major progress in water, sanitation, and hygiene indicators, most of the fight against cholera transmission has thus been conducted through the nationwide rapid response strategy, which was gradually implemented beginning in mid-2013 (6) and was shown to effectively shorten and mitigate cholera outbreaks in Haiti (9).

According to observational and experimental results from Bangladesh, vibriophages might play a role

in the natural control of cholera epidemics (10). Although a single phage isolation was reported in Haiti in 2013 (11), vibriophages might have influenced the seasonal dynamic of cholera. Whether they have also contributed to the epidemic collapse requires further investigation.

Because reports of long-term carriers of cholera are anecdotal and they have not been shown to trigger outbreaks (12), the critical issue now is whether the epidemic strain of *V. cholerae* O1 has settled in Haiti and could lead to the reemergence of cholera in the near future (13). This scenario explicitly informed the Elimination Plan, which required substantial progress in human development to limit the annual incidence rate of cholera to 0.01% of the population (2). According to the published literature (13,14), no epidemic strain seems to have been isolated in surface waters in Haiti since November 2015. Until then, environmental isolates had remained sporadic and usually concomitant to local cholera cases; therefore, differentiating a true environmental reservoir from a recent fecal contamination remains controversial (13,14). Cholera recurrence after lull periods might simply come from a low-grade and underreported persistent interhuman transmission (14) rather than from aquatic reservoirs (13).

Because cholera has not been reported in the neighboring Dominican Republic since 2018 (http://digepisalud.gob.do/documentos), the island of Hispaniola might now be located thousands of kilometers away from current transmission foci. In the past, numerous countries in Africa have experienced severe epidemics and prolonged remissions, despite low human development indices, and have remained free from cholera for years (e.g., 8 years for Guinea and 19 years for Madagascar). Similarly, the absence of cholera outbreaks in South America since the early

³³⁷²⁻App1.pdf). NA, not applicable; OCV, oral cholera vaccine. †The proportion of fully vaccinated population was calculated by dividing the number of persons who received the 2nd OCV dose by the population of Haiti. ‡Percentage of the population with residual vaccine immunity was estimated taking into account the number of vaccinated persons, the percentage of

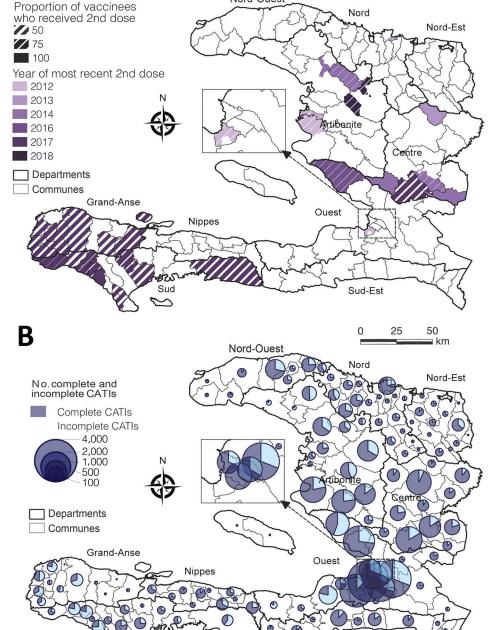
2000s, despite a large epidemic wave in the 1990s, is reason for optimism.

Until the certification of cholera elimination by the World Health Organization, systematic bacteriologic testing of every case of severe acute watery diarrhea, combined with environmental monitoring, should be maintained in Haiti. However, achieving 2.5 years with no deaths from cholera or confirmed cholera cases in

a country where the disease was considered impregnable is already a victory. This achievement should be considered a springboard to further understand cholera epidemics and improve control strategies worldwide. This success should foster investments in water, sanitation, and hygiene infrastructure, which will protect Haiti against possible future cholera epidemics and against other remaining waterborne diseases.

25

50 — km



Nord-Ouest

Figure 2. Cholera control in Haiti, 2012-2019. A) Oral cholera vaccine campaigns during 2012-2018 by subcommune; B) complete and incomplete CATIs conducted during July 2013-December 2019 by commune. Complete CATIs are defined by house decontamination, education, soap and chlorine distribution, and distribution of antibiotics to close contacts of cholera case-patients. Data source: Ministry of Public Health and Population of Haiti (pers. comm., 2021 Jul 20); UNICEF (pers. comm., 2020 Jan 20; see also Appendix, https://wwwnc. cdc.gov/EID/article/27/11/20-3372-App1.pdf). CATI, case-area targeted interventions.

Table 2. Suspected cholera cases and case-area targeted interventions, Haiti, 2012–2019*

Total no. suspected			No. (%)		
Year	cholera cases	No. CATIs	Complete CATIs†	Targeted communes	CATIs/case ratio‡
2012	101,503	ND	ND	ND	ND
2013	58,574	3,599	4 (0)	87 (62)	0.1
2014	27,392	3,241	434 (13)	125 (89)	0.1
2015	36,045	8,091	5,500 (68)	131 (94)	0.2
2016	41,421	13,031	10,869 (83)	138 (99)	0.3
2017	13,681	12,244	10,739 (88)	129 (92)	0.9
2018	3,777	6,561	5,525 (84)	83 (59)	1.7
2019	458	1,943	1,683 (87)	42 (30)	4.2
Total	181,348	48,710	34,754 (71)	139 (99)	0.3

^{*}Data source: UNICEF (pers. comm., 2020 Jan 20; see also Appendix, https://wwwnc.cdc.gov/EID/article/27/11/20-3372-App1.pdf). Exhaustive recording of CATIs by UNICEF started in July 2013 with the launch of the nationwide coordinated rapid response strategy. CATI, case-area targeted interventions; ND, no data

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[†]CATI with house decontamination, education, soap and chlorine distribution, and distribution of antibiotic drugs to contacts.

[‡]Ratio of the total number of CATIs by the total number of suspected cholera cases, per year.

Toward Cholera Elimination, Haiti

Appendix

Description of Cholera Surveillance System in Haiti

Since October 2010, cholera treatment facilities (between 136 and 262 cholera treatment centers, cholera treatment units, and acute diarrhea treatment centers, depending on the period) routinely recorded and notified cholera-associated illnesses and deaths. According to the World Health Organization standard definition (1), a probable cholera case was defined as acute watery diarrhea with or without vomiting in a patient >5 years of age. In Haiti, suspected cholera cases in children <5 years old with similar symptoms were also separately recorded and included in the global cholera toll. Daily suspected cases (both hospitalized and nonhospitalized), as well as daily suspected cholera deaths in health facilities and the community, were anonymously transmitted to 1 of the 10 department health directorates through formatted text message (2) or telephone call. Department directorates compiled and validated this data by using Microsoft Excel (https://www.microsoft.com), then sent the data to the national Directorate of Epidemiology Laboratory and Research, typically daily, albeit with frequent delays. The Directorate of Epidemiology Laboratory and Research validated departmental data and compiled the information into a national spreadsheet at a daily and communal scale before performing analyses. Commune records noted the treatment facility of cholera patients, not their place of residence. Community cases were not recorded. By January 2020, a total of 820,497 suspected cholera cases and 9,582 associated deaths had been recorded by the Ministry of Public Health and Population of Haiti (MOH).

Since 2010, routine bacteriologic confirmation of suspected cholera cases was performed at the National Laboratory of Public Health (LNSP) in Delmas, Haiti, by using standard sampling, culture, and phenotyping methods (3); the Centers for Disease Control and Prevention provided support. Since July 2017, a private laboratory run by the nongovernmental organization (NGO) Zanmi Lasante and located in Saint-Marc, Artibonite department, performed cultures of stool specimens with support of UNICEF and notified results to the LNSP. During October

2010–June 2021, a total of 24,610 stool specimens, mostly sampled using rectal swab specimens in Carry-Blair transport medium, have been included in the national microbiologic cholera surveillance system. Overall, 40.6% of the specimens were positive for *Vibrio cholerae* O1.

Brief Description of Cholera Control Interventions in Haiti

From 2012 onward, the MOH and its partners have organized several oral cholera vaccine (OCV) campaigns using 2-dose killed whole-cell OCVs: Shanchol (Shantha Biotechnics, https://www.sanofi.in), then Euvichol (Eubiologics, http://eubiologics.com). In 2012, 2 pilot campaigns were implemented in an urban neighborhood of the capital Port-au-Prince (4) and in a rural area of the Artibonite department (5). In the years after, several additional campaigns were conducted across the country, notably in Cap Haitien, the second largest city in the country, in 2013, and several highly affected communes of the central area (6,7). For fear of a cholera upsurge after Hurricane Matthew, which hit the southwestern tip of Haiti in October 2016, a large OCV campaign targeting >800,000 residents was launched in November 2016 in 18 communes of the Sud and Grande-Anse departments. However, the second dose was administrated only in May–June 2017. The last OCV campaign implemented in Haiti targeted several areas of Saint-Michel-de-l'Attalaye, a highly affected commune in the Artibonite department, in April–May 2018.

Beginning in July 2013, the nationwide case-area targeted rapid response strategy to eliminate cholera in Haiti was laboriously but increasingly implemented throughout the country (8). In all departments, UNICEF established partnerships with NGOs that hired water, sanitation, and hygiene rapid response teams composed of staff local to Haiti. The MOH also established its own teams called EMIRAs (Equipe mobile d'intervention rapide), which included healthcare workers (i.e., nurses and auxiliary nurses). Staff of the NGO rapid response teams and EMIRA worked together and deployed mixed teams, which were requested to respond to every suspected cholera case or death within 48 hours of admission to a healthcare facility. For this purpose, rapid response teams were encouraged to obtain lists of cholera cases on a daily basis from department health directorates and treatment centers (8). The core methodology of case-area targeted interventions (CATIs) had been established with the MOH and its partners and has been described elsewhere (8). In brief, it included door-to-door visits to affected families and their

neighbors; house decontamination by chlorine spraying of latrines and other potentially contaminated surfaces; onsite organization of education sessions about cholera and hygiene promotion; distribution of 1 cholera kit per household (composed of soaps, sachets of oral rehydration solution, and chlorine tablets; prophylactic antibiotics with doxycycline to contacts living with cholera case-patients; manual bucket chlorination at drinking water collection points, when appropriate; chlorinated water supply systems; supervision of safe funeral practices for cholera deaths; and primary care to cholera case-patients in the community. CATIs were prospectively documented and transmitted by water, sanitation, and hygiene rapid response teams to UNICEF with date, location (i.e., commune, communal section, and locality) and implemented activities, including specific activities of embedded EMIRA staff.

Data Collection and Analysis

We first used anonymous information of daily reported numbers of suspected cholera cases and deaths at the communal level (Ministry of Public Health and Population of Haiti, pers. comm., 2021 Jul 20); the study was authorized by the Bioethics National Committee of the MOH (authorization no. 1819–41). Annual population estimates were extrapolated from the 2012 and 2015 estimates provided by the Haitian Institute of Statistics and Informatics (9,10). We then computed annual cholera incidence rates. We also manually searched the database for most recent clusters of suspected cholera cases and compared that data with prospective weekly cholera epidemiologic bulletins of the MOH

(https://mspp.gouv.ht/newsite/_direction/pageDocumentation.php?IDDir = 9, cited 2020 Dec 14). For each commune, we computed the time elapsed since the last recorded suspected cholera case.

As prevalence of cholera decreases, the predictive positive value of the clinical definition for suspected cholera cases weakens (11), and stool culture surveillance for Vibrio cholerae O1 becomes more vital to follow the dynamic of the epidemic. We thus analyzed the LNSP database of cholera stool cultures (Ministry of Public Health and Population of Haiti, pers. comm., 2021 Jul 20) and plotted the weekly number of positive and negative cultures, as well as the monthly culture-positivity rate. For each of the administrative communes of Haiti, we also calculated the time since the last positive stool culture, time since the last negative culture, and the number of

consecutive negative cultures since the last positive one. We also calculated the time since the last suspected cholera death and the last suspected cholera case. We then classified the surveillance effort for each commune and calculated the time since possible cholera elimination accordingly (Appendix Table). Finally, we counted the number of communes with possible cholera elimination for ≥ 3 years, which corresponds to the definition of cholera elimination according to the Global Task Force on Cholera Control (12), and mapped these indicators (Appendix Table).

To analyze factors associated with the cholera dynamic, we summarized OCV campaigns recorded by the MOH, including date, place at the subcommunal level (called section communale in Haiti), number of persons who received ≥1 dose, and number of persons who received 2 doses. We mapped these OCV campaigns at the subcommunal level, illustrating the administration year of the 2nd dose and the proportion of vaccinees who received the 2nd dose. By using Haitian Institute of Statistics and Informatics demographic estimates, we approximated the proportion of the population in Haiti who were fully vaccinated since 2012. Because protection of OCVs decreases over time (13), we approximated the annual proportion of the population with residual vaccine immunity by multiplying the number of persons vaccinated during each campaign by the published vaccine effectiveness for a 2-dose regimen (56% the first year, 59% the second year, 39% the third year, and 24% the fourth year) and 1-dose regimen (40% the first year) (13). We considered effectiveness dropped to 0% after these delays.

Finally, we summarized CATIs recorded by UNICEF between the onset of the nationwide strategy in July 2013 and December 2019 (UNICEF, pers. comm., 2020 January 20). We counted the number of CATIs by commune and by year, as well as the number and proportion of CATIs that involved a complete package of house decontamination by chlorine spraying, health education about cholera, distribution of soap and chlorine tablets for household water treatment, and distribution of antibiotic prophylaxis to close contacts of cholera casepatients. We then mapped the number of CATIs by commune with the proportion of complete CATIs. To assess the evolution of the relative response effort to suspected cholera cases, we calculated the annual ratio of the total number of CATIs to the total number of suspected cholera cases.

Data management was performed using Microsoft Excel for Mac version 16.45. QGIS version 3.8 (http://www.qgis.org) was used to draw the maps.

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Appendix Table. Category of cholera surveillance effort and associated definition of the time since possible cholera elimination, by commune.

		Definition of the time since possible cholera
Categ	ory of cholera surveillance effort	elimination
(a)	Communes with ≥1 negative culture since the last positive culture or the last reported death	Time elapsed since the last positive culture or suspected cholera death
(b)	Communes with no culture since the last positive one or the last reported death	Time since the last reported suspected cholera case or death
(c)	Communes with no history of stool sampling for cholera culture but with reported cases	Time since the last reported suspected cholera case or death
(d)	Communes with no history of stool sampling and no reported cases	No definition